

LBA86

Randomised phase III trial of androgen deprivation therapy (ADT) with radiation therapy with or without enzalutamide for high risk, clinically localised prostate cancer: ENZARAD (ANZUP 1303)

P.L. Nguyen¹, C. Sweeney², M.R. Stockler³, H. Thomas³, B. Mak³, A. Zhang³, T.S. Lim⁴, C.C. Jose⁵, J. Martin⁶, N. Patanjali⁷, D. Pryor⁸, P. Tran⁹, S. Mangar¹⁰, A.M. Mihai¹¹, M. Beresford¹², F. Sedlmayer¹³, P.J. Kelly¹⁴, S. Hughes¹⁵, I.D. Davis¹⁶, S. Williams¹⁷

¹ Radiation Oncology, Mass General Brigham, Harvard Medical School, Boston, United States of America, ² South Australian Immunogenomics Cancer Institute, The University of Adelaide, Adelaide, Australia, ³ NHMRC Clinical Trials Centre, The University of Sydney, Camperdown, Australia, ⁴ Department of Radiology, Genesis Cancer Care, Fiona Stanley Hospital, Perth, Australia, ⁵ Radiation Oncology, Auckland City Hospital, Auckland, New Zealand, ⁶ Department of Radiation Oncology, Calvary Mater Newcastle, Waratah, Australia, ⁷ RPA, Royal Prince Alfred Hospital, Camperdown, Australia, ⁸ Department of Radiology, Princess Alexandra Hospital, Woolloongabba, Australia, ⁹ Radiation Oncology, GenesisCare, Kurralt Park, Adelaide, Australia, ¹⁰ Clinical Oncology, Charing Cross Hospital - Imperial College Healthcare NHS Trust, London, United Kingdom, ¹¹ Radiotherapy, UPMC Beacon Hospital, Dublin, Ireland, ¹² Clinical Trials, Royal United Hospitals Bath - NHS Foundation trust, Bath, United Kingdom, ¹³ Radiation Oncology, Paracelsus Medizinische Privatuniversität, Salzburg, Austria, ¹⁴ Radiotherapy, Bon Secours Hospital, Cork, Ireland, ¹⁵ Clinical Trials, Guy's & St Thomas NHS Foundation Trust, London, United Kingdom, ¹⁶ Eastern Health Clinical School, Eastern Health Clinical School - Monash University, Box Hill, Australia ¹⁷ Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

Background

We evaluated the effects of adding enzalutamide (ENZA) to standard adjuvant ADT with radiation therapy (RT) for high-risk, localised or locally-advanced prostate cancer (L/LAPC).

Methods

Participants (pts) having 24mo ADT and RT for high-risk L/LAPC were randomized to ENZA 160mg daily for 24 mo vs a non-steroidal anti-androgen (NSAA) for 6 mo with stratification across 7 clinico-pathological factors. Metastasis-free survival (MFS) on conventional imaging (ICECaP) was the primary endpoint. Secondary endpoints included OS, PC-specific survival (PCSS), PSA progression-free survival (PSA-PFS), clinical-PFS, and adverse events (AE). 200 MFS events provided 80% power assuming a true MFS hazard ratio (HR) of 0.67 and 2-sided alpha of 0.05. Main effects were tested with unstratified logrank p-values. Five subgroups of interest were prespecified and subgroup effects were tested with interaction p-values (i-p).

Results

We enrolled 802 pts from MAR2014 to JUN2018: median age 71; 89% Gleason 8-10; 47% T3-4; 35% PSA $\geq$ 20; and 11% N1. 207 MFS events occurred during a median follow-up of 92 mo. ENZA and NSAA had similar effects on MFS, OS, and PCSS; ENZA had larger effects on PSA-PFS and clinical-PFS (Table). Effects of ENZA on MFS were larger in 2 of the 5 pre-specified subgroups of interest: clinical N1 (i-p=0.04) and planned pelvic RT (i-p<0.001), but not in the very-high-risk (cN1 or Grade Group (GG) 5 or GG 4 with cT2b-4 or PSA >20 ng/mL), Age<70, or by region. The AEs reported for most pts (ENZA vs NSAA) were fatigue (353 vs 321), hot flashes (315 vs 281), and urinary frequency (309 vs 303). Grade 3-5 AEs occurred in 185 pts in each group.

Conclusions

The addition of ENZA to ADT and RT had limited effects on MFS during 8 years of follow-up in high-risk L/LAPC. Effects on MFS were larger in those with positive pelvic nodes on conventional imaging, and in those with pelvic RT planned. Clinical trials information: NCT02446444. Table: LBA86

Outcome at 8 years	ENZAN=401	NSAAN=401	HR (95% CI)	p-value (2-sided)
MFS	74%	72%	0.88 (0.67, 1.15)	0.34
OS	83%	80%	0.87 (0.63, 1.20)	0.40

Outcome at 8 years	ENZAN=401	NSAAN=401	HR (95% CI)	p-value (2-sided)
PCSS	97%	96%	0.90 (0.41, 1.97)	0.79
PSA-PFS	67%	62%	0.78 (0.61, 0.99)	0.04
Clinical-PFS	72%	66%	0.76 (0.59, 0.98)	0.04
MFS at 8 years in 2 of 5 prespecified subgroups of interest (Also stratification factors)	Interaction p-values (2-sided)			
N1 subgroup	77% (N=46)	50% (N=42)	0.43 (0.20-0.92)	0.04
N0 subgroup	74% (N=355)	75% (N=359)	0.97 (0.72-1.30)	
Pelvic RT subgroup	82% (N=162)	65% (N=162)	0.47 (0.29-0.76)	<0.001
No pelvic RT subgroup	69% (N=239)	76% (N=239)	1.25 (0.89-1.76)	

Clinical trial identification

NCT02446444.

Legal entity responsible for the study

The Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP).

Funding

The Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP).

Disclosure

P.L. Nguyen: Financial Interests, Personal, Other, Consulting: Boston Scientific, Johnson and Johnson, MDx Health, Novartis, AIQ, Nanocan; Financial Interests, Personal, Stocks/Shares: Nanocan, Stratagen Bio; Financial Interests, Personal, Ownership Interest: Reversal Therapeutics; Non-Financial Interests, Leadership Role, NRG GU Group Leader: NRG Oncology. C. Sweeney: Financial Interests, Personal, Advisory Board, Consultancy: Genentech_Roche, Bayer, Astellas, Pfizer; Financial Interests, Personal, Other, Consultancy: Janssen, MSD, Novartis, Amgen; Financial Interests, Personal, Advisory Board: Point, Cellcentric; Financial Interests, Personal, Advisory Board, Consultant: Advancell; Financial Interests, Personal, Advisory Board, Advisory Boards: BMS; Financial Interests, Personal, Advisory Board, Consulrant: Amphista; Financial Interests, Personal, Stocks/Shares: Leuchemix; Financial Interests, Personal, Stocks/Shares, Consultant: Advancell; Financial Interests, Institutional, Advisory Board, Abiraterone plus cabozantinib: Exelixis; Financial Interests, Institutional, Research Grant: Bayer, Janssen, Astellas, Pfizer, Dendreon, Sanofi. M.R. Stockler: Financial Interests, Institutional, Research Grant, DASL: Bayer; Financial Interests, Institutional, Research Grant, ENZAMET & ENZARAD: Astellas; Financial Interests, Institutional, Research Grant, KEYPAD: Amgen, MSD; Financial Interests, Institutional, Research Grant, NIVORAD: BMS; Financial Interests, Institutional, Research Grant: Pfizer, ROCHE; Financial Interests, Institutional, Research Grant, ADELE: BeiGene; Financial Interests, Institutional, Research Grant, PARAGON2: NOVARTIS; Financial Interests, Institutional, Other, Study Drug for Cannabis CINV Trial: Tilray; Financial Interests, Institutional, Research Grant, ILLUMINATE, PHAEDRA.: AstraZeneca. A. Zhang: Financial Interests, Personal, Advisory Board: Merck Sharpe Serono, Astellas, Pfizer, Merck, Bayer, Janssen, Bristol Myer Squibb; Financial Interests, Personal, Invited Speaker: Merck Sharpe Serono, Astellas, Janssen, Ipsen, Bayer; Non-Financial Interests, Principal Investigator: Astellas, Merck Sharpe Serono, TYRA therapeutics, Bristol Myers Squibs; Non-Financial Interests, Member: American Society of Clinical Oncology, Medical Oncology Group of Australia, Australia and New Zealand Urogenital and Prostate (ANZUP) grop. J. Martin: Financial Interests, Personal, Advisory Board: Astellas; Financial Interests, Personal, Officer, Chief Medical Officer: SeeTreat; Financial Interests, Personal, Stocks/Shares: GenesisCare, SeeTreat, MarginClear; Financial Interests, Institutional, Research Grant, Research grant for a clinical trial in oesophageal cancer: Varian. D. Pryor: Financial Interests, Personal, Invited Speaker, Educational Meeting Speaker March 2023: Bayer; Financial Interests, Personal, Invited Speaker, Educational meeting speaker November 2021: AstraZeneca; Financial Interests, Personal, Full or part-time Employment, Part time visiting medical officer for private health care provider: Icon Cancer Care. M. Beresford: Financial Interests, Personal, Advisory Board: Pfizer, AstraZeneca, Roche, Gilead, Genesiscare; Financial Interests, Personal, Invited Speaker: Novartis. P.J. Kelly: Financial Interests, Personal, Invited Speaker, Delivered a talk on bone health in prostate cancer June 2024: Amgen; Financial Interests, Personal, Advisory Board, Medical opinions for defence council in medicolegal cases: States Claims Agency, Ireland; Financial Interests, Personal, Advisory Board, Barrigel ad board Estro 2025: Teleflex; Financial Interests, Personal, Other, Advisory contract: Boston Scientific; Financial Interests, Personal, Other, Travel support to attend

ESTRO annual meeting 2025: Accord; Financial Interests, Personal, Other, Travel support to attend GU ASCO Meeting 2025: Pfizer. S. Hughes: Financial Interests, Personal, Invited Speaker, Ran an education seminar on prostate cancer for trainees at 2 national events: P3 2024 meeting; P3 2025 meeting: Bayer; Financial Interests, Personal, Invited Speaker, Co-Chair / organiser for the Annual PROSPECT Prostate and Bladder Cancer Meeting: 2024; 2025: Astellas; Financial Interests, Personal, Invited Speaker, Gave a talk on the prostate cancer diagnostic pathway to Janssen staff: 2025: Janssen; Financial Interests, Personal, Invited Speaker, Panel member at an educational webinar on PSMA Lutetium: 2025: Novartis; Financial Interests, Institutional, Other, Unrestricted grant to run a webinar and a multidisciplinary training day on the management of advanced bladder cancer: 2025 (Astellas had no input to the content): Astellas; Financial Interests, Personal, Full or part-time Employment, I'm the Clinical Lead for Radiotherapy and chair the SABR multidisciplinary meeting: TheLondon Clinic (Charity); Financial Interests, Personal, Ownership Interest, I'm co-founder and co-CEO of The Learning Lab - a Digi-tech company: The Learning Lab; Non-Financial Interests, Other, Member of the Education Council; Course leader for various international education activities: ASCO. I.D. Davis: Financial Interests, Personal, Full or part-time Employment, Professor of Medicine and Head of Eastern Health Clinical School: Monash University; Financial Interests, Personal, Full or part-time Employment, Professor of Medicine; Head, Eastern Health Clinical School; medical oncologist: Eastern Health; Financial Interests, Institutional, Local PI, Institutional support for clinical research: Movember Foundation, Merck/MSD, Bristol Myers Squibb, Exelixis, Astellas, Pfizer, AstraZeneca, Roche / Genentech, Eisai, Bayer, Janssen, Ipsen, Seagen; Financial Interests, Institutional, Local PI, EPI-7386-CS-010 trial: ESSA Pharma; Non-Financial Interests, Member of Board of Directors, Director and Chair; unremunerated: ANZUP Cancer Trials Group; Non-Financial Interests, Advisory Role, All honoraria and payments are made directly to ANZUP Cancer Trials Group with no pass-through payment: Roche, Eisai, Xennials Therapeutics, Telix Therapeutics, AstraZeneca, Bayer; Non-Financial Interests, Other, Member of Council: Clinical Oncology Society of Australia; Non-Financial Interests, Member: ASCO, Clinical Oncology Society of Australia, Medical Oncology Group of Australia, American Association for Cancer Research, Australian Academy of Health and Medical Sciences, Australian Society for Medical Research, American Association of Immunologists. All other authors have declared no conflicts of interest.

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